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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,885	11/10/2006	Marshall David Crew	0003.0553/PC32027A	1858

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EXAMINER	
SOROUSH, ALI	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
03/23/2012	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,885	CREW ET AL.	
	Examiner	Art Unit	
	ALI SOROUSH	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *20 and 22-37* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *20 and 22-37* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Receipt

Applicant's response filed on 01/10/2012 to the Office Action mailed on 10/13/2011 is acknowledged.

Claim Status

Claims 20 and 22-37 are pending.

Claims 1-19 and 21 are previously cancelled.

Claim 20 is currently amended.

Claim 35-37 are newly added.

Claims 20 and 22-37 have been examined.

Claims 20 and 22-37 are rejected.

Claim 37 is objected to.

Priority

Priority to PCT/IB04/04260 filed on 12/20/2004 which claims priority to application 60/533848 filed on 12/31/2003 is acknowledged.

Claim Objections

This is a new objection necessitated by amendment.

Claim 37 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim shall refer to other claims in the alternative only. See MPEP § 608.01(n). In the interest of compact prosecution the claim has been interpreted to

recite, “The solid composition of claim 35 or 36, wherein the amount of said poloxamer in said particles is 30 to 65%."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejection is reiterated from the Office Action mailed on 10/13/2011.

1. Claims 20, 22-34, and **newly added claims 35-37** are rejected under 35 U.S.C. 103(a) as being unpatentable over Infeld et al. (International Application Published Under the PCT WO 02/089835 A2, Published 11/14/2002) in view of Babcock et al. (European Patent Application 1027886 A2, Published 08/16/2000).

The claims are directed to solid composition comprising particles of at least 10% low-solubility amorphous drug, 30 to 65% poloxamer, and a at least 5% stabilizing polymer such as hydroxypropyl methyl cellulose acetate succinate (HPMCAS). The claims are further directed to an anti-viral drug. The claims are further directed to the amount of HPMACS being present such that the MDC of the drug is increased at least 1.25 fold over a control.

Infeld et al. show a tablet comprising a kernel having 61.3% nelfinavir mesylate (chemical name: N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-3-isoquinoline carboxamide monomethanesulphonate), 33.1% poloxamer 188, 3.4% microcrystalline cellulose, corn starch, and magnesium stearate. (page 12, example 5). Nelfinavir mesylate is an low-soluble, amorphous, hydrophobic antiviral drug. (page 1, Lines 5-28). The drug kernel is

made by melt granulation process which results in the formation of particles. (page 6, Lines 7-15). The presence of poloxamer enhances the bioavailability of the drug. (page 2, Lines 15-16).

Infeld et al. lacks a teaching wherein the particles further comprise a stabilizing polymer such as hydroxypropyl methyl cellulose acetate succinate (HPMCAS).

Babcock et al. show a solid dispersion of a low-solubility drug and a polymer. (abstract). The preferred polymer is cellulosic. (page 29, Lines 19-36). The most preferred polymer is the stabilizing polymer HPMCAS. (page 33, Lines 23-27, prior art claim 57). HPMC will stabilize amorphous low-soluble drugs so that they do not undergo change to crystalline form overtime during storage. (page 3, Lines 5-14). This dispersion provides an MCD and AUC of 1.25 fold over a control composition. (page 7, Lines 17-30). In preferred embodiment 30% HPMACS is present in an example dispersion (page 18, lines 20-25).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the composition of Infeld et al. by adding HPMCAS taught by Babcock et al. to the composition. One of ordinary skill in the art would have been motivated to do so in order to provide enhanced stability to the tablet formulation of Infeld et al. With regard to the instantly claimed glass transition temperature of the particle and drug as instantly claimed, it would be expected that the particles taught by Infeld et al. as modified by Babcock et al. would also possess this property. With regard to the instantly claimed method of making the composition, this is a product-by-process limitation that is not given patentable weight in a product claim.

Response to Applicant's Arguments

Applicant argues that there is not teaching or suggestion in Infeld et al. that the nelfinavir compositions require any stabilization let alone stabilization by a cellulosic polymer such as HPMCAS or CMEC. Applicant's argument has been fully considered but found not to be persuasive. Infeld et al. teach that stabilizers may optionally be added to the composition. Further Babcock et al. teach that addition of cellulosic stabilizers such as HPMCAS will increase the MCD and AUC by 1.25 over a control composition. Therefore, it is Babcock et al. which provides the suggestion of adding HPMCAS to the composition of Infeld et al.

Applicant argues that the Examiner reasons that HPMCAS is preferred stabilizing polymer since Babcock et al. teach that cellulosic polymers are preferred, but that in fact Babcock et al. make it clear that HPMCAS is not suitable for stabilizing the composition alone. Applicant's argument has been fully considered but found not to be persuasive. Babcock et al. clearly teach that HPMCAS is a stabilizing polymer that is preferred, on page 33 in prior art claim 57 Babcock et al. recites, "The composition of claim 54, wherein the **stabilizing polymer is selected from the group consisting of** ... **hydroxypropyl methyl cellulose acetate phthalate** ..." Therefore, there is no ambiguity as to whether Babcock et al. teach HPMCAS as a stabilizing polymer.

Applicant argues that the claims Applicant further argues that claim 20 recites "consisting of HPMCAS and CMEC" and therefore is limited to the inclusion of a polymer that is either hPMCAS alone or CMEC alone. Applicant's argument has been fully considered but found not to be persuasive. **This is a Markush style claim**

limitation and not a limitation on the contents of the composition. The limitation on the claim is only to the type of stabilizing polymer that must be added to the composition and not what additional constituents the composition may consist of. The claims have been amended to recite that composition "consists essentially of". "By using the term 'consisting essentially of,' the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention. A 'consisting essentially of' claim occupies a middle ground between closed claims that are written in a 'consisting of' format and fully open claims that are drafted in a 'comprising' format." *PPG Industries v. Guardian Industries*, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355. Therefore, even assuming arguendo that in order to stabilize a composition with HPMCAS, Babcock et al. teach that CAP must also be added, the teachings of Infeld et al. and Babcock et al. suggests the instantly claimed limitations.

Applicant argues that Babcock et al. does not reference HPMC or HPMCAS at page 3, lines 5-14. Applicant is correct, the Examiner points to this section only to show what Babcock et al. intends when reciting the term stabilize and that since these compounds are taught to stabilize, they would necessarily act in such a manner.

For the forgoing reasons the rejection is maintained.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALI SOROUSH whose telephone number is (571)272-9925. The examiner can normally be reached on M-F (9am-6pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun G. Sajjadi can be reached on (571)272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ALI SOROUSH/
Examiner, Art Unit 1617

/KARLHEINZ R SKOWRONEK/
Primary Examiner, Art Unit 1631

Wednesday, March 14, 2012